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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,544	05/04/2001	Ronald A. Faris	21486-024	2853

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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	7

DATE MAILED: 09/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/743,544	FARIS, RONALD A.
	Examiner	Art Unit
	Joseph T. Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 03 June 2002.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-48 is/are pending in the application.

4a) Of the above claim(s) 1-34 and 42-48 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 35-41 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____

2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) Other: _____

DETAILED ACTION

This application is a 371 national stage filing of PCT/US99/15625, filed July 8, 1999, which claims benefit of 09/113,774, file July 10, 1998, now US Patent 6,129,911.

Election/Restriction

Applicant's election without traverse of group III, claims 35-41, in Paper No. 6 is acknowledged. Claims 1-48 are pending. Claims 1-34 and 42-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 6. Claims 35-41 are currently under examination.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Amending the first line of the specification to recite the priority information set forth above would satisfy the requirement.

Art Unit: 1632

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

It is noted that declaration was amended to indicate the Inventors new address as of 12/25/01, however it is unclear when this amendment was made. The Inventor signed the declaration 4/23/01, however he did not initial the change of address.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required if the application is allowed.

Specification

The abstract of the disclosure is objected to because the present application does not contain an abstract. The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be

Art Unit: 1632

presented on a separate sheet, apart from any other text. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 35 recites the limitation "said doublet" in step (c) of the method. There is insufficient antecedent basis for this limitation in the claim. Dependent claims 36-41 are included in the basis of the rejection because they fail to clarify the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1632

Claims 35-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Reid *et al.* (WO 93/03142).

Claims 35-38 are drawn to a method of obtaining a liver stem cell comprising isolating a cluster of cells from the liver and separating the hepatocytes from the stem cell. The size and nature of the cluster are not specifically defined in the claims, and can be interpreted to encompass a cluster of cells as in a section of liver. More specifically, because a cluster is not precisely defined and in light of the teachings in the specification can comprise many cells, a portion of a liver removed from an animal could be interpreted as comprising a cluster of cells. Further, because of the open language of the claims, in claim 37 though isolation of a cluster comprising a doublet is claimed, because the doublet can be comprised in a larger population of cells such as a liver section, this claim is also included in the basis of the rejection. Reid *et al.* describe methods for isolating and culturing liver progenitor cells. Reid *et al.* do not use the term "liver stem cell" as recited in the instant claims, however the definition and characteristics of a liver progenitor cell defined by Reid *et al.* comprises all the characteristics of a liver stem cell as set forth in the present specification. Therefore, a liver stem cell and progenitor cell are being interpreted as encompassing the same cell. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Luditke*. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35

Art Unit: 1632

USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, Reid *et al.* teach that a liver progenitor cell can be enriched from a section of liver. The hepatocytes and stem cells can be isolated one from the other by using selective culturing conditions (page 3). Because the liver progenitor cell is isolated from a section of liver, the portion of the claim reciting isolating a cluster is considered to be met. Finally, though Reid *et al.* do not provide a detailed analysis of the resulting isolated cells, because the methodology used encompasses that generally taught in the present specification and using these methods results in a liver progenitor cell, the cells resulting from practicing the methods of Reid *et al.* would anticipate an isolated liver stem cell as presently claimed.

Thus, the methods taught by Reid *et al.* for the isolation of a liver progenitor cell anticipate the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

Art Unit: 1632

to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reid *et al.* in further in view of Sell (Cancer Research, 1990) and Alison (Current Opinions in Cell Biology, 1996).

Claims 39-41 are drawn to methods where specific cell markers of a cell are recited. The teaching of Reid *et al.* is summarized above. Reid et al. teach the isolation of liver progenitor cells, however they do not teach any of the specific cell markers recited in claims 39-41. Sell and Alison review the state of the art regarding liver stem cells and describe several of the specific markers in the instant claims (Sell page 3811, second column, and Alison, Table 1 and Figure 1). Neither teach to use these markers as a means to isolate liver stem cells, however they clearly teach that they represent markers present on specific types of cells found in the liver. Reid et al. teach several methods of isolating liver stem cells, and among the specific methodologies discussed, Reid *et al.* suggest using antibodies to separate specific cell types one from the other (pages 2-3, bridging paragraph). In light the specific suggestion of Reid *et al.* to use antibodies it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the specific cell markers and antibodies for these markers as taught in Sell and Alison in methods to obtain a more purified population of liver stem cells. One having ordinary skill in the art would have been motivated to use the specific cell surface markers and antibodies taught in Sell and Alison in the methodology suggested by Reid et al. The use of

Art Unit: 1632

antibodies to identify and isolate cells was well known in the art, and commonly used to obtain a specific cell of interest, and in view of the ability of the specific antibodies to recognize specific cell types within the liver as demonstrated by Sell and Alison, there would have been a reasonable expectation of success to use the antibodies discussed in Sell and Alison in the methodology described in Reid et al. to identify a cell with each of the specific marker recited in the claims.

Thus, absent evidence to the contrary, the claimed invention as a whole was clearly *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

Art Unit: 1632

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 35-41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 35-44 of U.S. Patent No. 6,129,911 ('911). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method set forth in the patent is encompassed by the instant claims. In each specification the metes and bounds of what is considered a cluster of cells is specifically defined. The claims '911 patent recites that the cluster is less than 10 cells, however dependent claim 37 indicates that the cluster is comprised of only a doublet which is the same limitation recited in claim 37 of the present application. In view of the minimum limitation of a cell doublet, and in view of the teaching of each of the specification for a cell cluster, any higher range limit would be considered an obvious variant as long as at least the doublet is present. The limitations of specific markers are set forth in dependent claims are exactly the same in both claim sets.

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Malhi *et al.* Journal of Cell Science 115:(13):2679-2688 (July, 2002).

Art Unit: 1632

Dabeva *et al.*, Society for Experimental Biology and Medicine 204:242-252 (1993).

Yasui *et al.*, Hepatology 25:329-334 (1997).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

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